REMARKS

I. Status of the Claims

Petition for Reconsideration of Restriction related to claims 51-55 has been granted. Claims 19-21, 27-33 and 51-56 were pending prior to the Office Action dated June 22, 2004. Thus claims 19-21, 27-33, and 51-56 are currently pending. Claims 19-21, 30, 31, and 51-55 are herein amended. Support for amended claim 19 can be found at least on page 6, line 23 to page 7 line 4 and page 12, lines 16-20. Support for amendments to claims 20 and 21 can be found at least on page 6, lines 4-14 and pages 12-14. Further, support for claims 30 and 31 can be found at least on page 7, lines 1-4 and page 24, lines 5-11. Still further, support for claims 51-55 can be found at least on page 24, lines 5-11, pages 12-14, and pages 32-33.

II. Petition for Reconsideration of Claims 51-55

The Examiner alleges that Applicants have provided a false representation of fact in the Petition for Reconsideration of Restriction. The Examiner states that the sequence set forth in SEQ ID NO:2 does not contain all of the sequence set forth by SEQ ID NO:1 since the former is DNA while the latter is RNA. Applicants disagree with the Examiner's allegations of false representation. Applicants' assertions regarding the relationship between SEQ ID NO:1 and SEQ ID NO:2 are correct.

One of skill in the art is well aware of the direct biological and chemical relationship between an RNA sequence and a DNA sequence. In the textbook *Biochemistry*, the authors state "RNA may be sequenced by determining the sequence of its corresponding cDNA or by directly sequencing it by a variation of the chemical cleavage method." (Voet and Voet, Biochemistry, 1990, page 847, left column, end of first full paragraph, Appendix A). A polynucleotide

sequence is not substantively altered by it being represented in the context of an RNA sequence in the stead of a DNA sequence or vice-versa, due to the fact that the sequences differ in the substitution of very similar nucleotide bases with similar base-pairing characteristics, the pyrimidine uracil "U" for the pyrimidine thymine "T." In fact, when the RNA sequence of SEQ ID NO:1 is used as a query in a nucleotide database (*e.g.*, GenBank) using the BLAST program (www.ncbi.nlm.nih.gov/BLAST/) corresponding DNA sequences in the database are identified (Appendix B). Furthermore, Applicants state on page 6, lines 5-7 of the specification that "It is contemplated that the polynucleotide may be a DNA molecule or it can be an RNA molecule." and on page 11, lines 16-17 "As used herein, the term "polynucleotide" refers to an RNA or DNA molecule..." One of skill in the art, whether the sequence was represented as a DNA or an RNA, would readily identify the polynucleotide sequence of SEQ ID NO:1 and its inclusion within the polynucleotide sequence of SEQ ID NO:2. Thus, SEQ ID NO:2 does contain all of the sequence information of SEQ ID NO:1, as shown in the sequence listing and described on page 6 of the specification.

Claims 51-55 have been amended to depend from claim 31 and incorporate the limitations of claim 19, from which claim 31 depends, these claims are directed to polynucleotides whose sequence is similar in that they both contain the newly defined 3' GBV-B sequence of SEQ ID NO:1. Hence, no additional search would be required by the Examiner for claims 51-55 should claim 19 be found allowable, because of the overlap in sequence with independent claim 19, *i.e.*, SEQ ID NO:1. Thus, if claim 19 is allowable then any additional sequence would not affect the patentability of claims 51-55, in fact claims 51-55 are drawn to a further limitation of claim 19. Applicants retain the right to have a reasonable number of species examined, should the elected species be found patentable.

In light of the foregoing, the Applicants respectfully request that the Examiner withdraw the allegation of false representation of fact.

III. Claims 51-55 Satisfy 35 U.S.C. §112, Second Paragraph

Claims 51-55 are rejected under 35 U.S.C. §112, second paragraph, as being vague and indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Applicants respectfully traverse the rejection.

Claims 51-55 have been amended to depend from presently amended claim 31 to further clarify the relationship between the RNA and DNA based polynucleotides encoding the viral genome. As stated on page 3, line 19 of the specification, GBV-B is a flavivirus. Viruses of this family (*Flaviviridae*) are positive-sense RNA viruses (Fields Virology, 1990; Appendix C). The flavivirus genome is a positive-sense RNA molecule containing a single reading frame that is translated by a host cell into a polyprotein. The polyprotein is then subsequently processed to form viral components. Thus, splicing of the RNA or the presence of any early viral proteins are not required for viral replication and production. Being that the presence of a positive-sense RNA initiates the viral lifecycle in a host cell, either a DNA expressing such an RNA or introduction of the RNA directly into a host cell is sufficient for production of a virus (*e.g.*, specification at page 5, lines 20-23; Fields Virology, 1990 at page 934 (Appendix C)). Thus, any person skilled in the art of virology or related disciplines, in light of the specification, would readily recognize the operability of both DNA and RNA forms of the subject nucleic acids disclosed and claimed in the present application. Based on the foregoing, one of skill in the art would be enabled to make and use the invention as claimed.

Withdrawal of this rejection is respectfully requested.

IV. Claims 19-21, 27-33 and 51-56 Satisfy 35 U.S.C. §112, First Paragraph, Written Description Requirement

Claims 19-21, 27-33 and 51-56 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse the rejection.

Pending claim 19 has been amended to read as follows:

> 19. A method of producing a GBV-B derived virus comprising: introducing into a host cell a recombinant viral genome comprising a 3' terminal sequence of GBV-B, wherein the 3' terminal sequence comprises 50 contiguous nucleotides from SEQ ID NO:1; and culturing said host cell under conditions permitting production of a virus from said genome.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail so that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. (*Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116 (Fed. Cir. 1991)).

It is well known to one of skill in the art that the family *Flaviviridae*, which includes GBV-B virus, are positive strand RNA viruses with similar genomic organization (Fields Virology Chapter 30, page 934, at least; Appendix C). As described on page 51 of the present specification, components of one flavivirus may be substituted for those from another member of the family. Furthermore, various exemplary derivations of GBV-B virus are described throughout the Examples section of the specification, pages 32-61. In light of the written description standard, one of ordinary skill in the art would be able to understand that the claimed

invention encompasses methods for producing a GBV-B derived virus as provided in the pending claims.

The claims, as amended herein, are directed to such a "method of producing a GBV-B derived virus." One of ordinary skill would understand that a GBV-B derived virus is a virus produced from or a derivative of one or more flaviviral genomes based on GVB-B virus. The viral genome of GBV-B and other flaviviruses contain a single reading frame encoding a polyprotein. Applicants note that it is evident in the art that there is no requirement for viral early proteins to establish viral replication of this type of virus.

Claim 19 recites "introducing into a host cell a recombinant viral genome comprising a 3' terminal sequence of GBV-B" and "culturing said host cell under conditions permitting *production of virus* from said genome." (emphasis added). Description of an example of the subject matter in the pending claims is provided at least on page 6, line 23 to page 7, line 4. Examples 5 and 6, at pages 38-42 of the specification describe examples of construction and introduction of a GBV-B derived viral genome into host cells. In addition, the 3' terminal sequence of a GVB-B virus is described in the specification at least in FIG. 1; on pages 5, line 20 to page 6, line 2; page 9, lines 3 to 19; throughout the examples section, pages 32 to 61, and in SEQ ID NO:1. Furthermore, an example of the 3' terminal sequence in the context of the sequence of a viral genome of a member of the family *Flaviviridae* (GBV-B) is provided in SEQ ID NO:2. Thus, a virus produced from introducing a GBV-B derived viral genome comprising a 3' terminal sequence of GBV-B is described in the specification and would be understood by one of ordinary skill in the art to include a viral genome that, when introduced into a host cell, produces a GBV-B derived *virus*.

Thus, in light of the aforementioned, claims 19-21, 27-33 and 51-56 satisfy the written description requirement of 35 U.S.C. §112, first paragraph. Applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 USC §112.

CONCLUSION

Applicants believe that the foregoing remarks fully respond to all outstanding matters for this application. Applicants respectfully request that the rejections of all claims be withdrawn so they may pass to issuance.

The Examiner is invited to contact the undersigned patent agent at 713-651-5391 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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Date: 10/22/2009